MECHANISMS OF REGULATION OF NEUROPEPTIDE EXPRESSION AFTER NEURONAL INJURY, R. E. Zigmond, Dept. of Neurosciences, Case Western Reserve University, Cleveland, OH 44106-4975

The pattern of peptide expression in many neurons remains plastic into adulthood. Interestingly, the most dramatic changes have been observed under conditions where these peptides may have neurotrophic actions, namely after axonal damage, when a neuron is deprived of its supply of target-derived trophic factors. This phenotypic plasticity has been examined primarily in the peripheral nervous system (in sympathetic, sensory and motor neurons); and the exact nature of the alterations in peptide expression differ between neuronal cell types. In normal animals, about 60% of the neurons in the superior cervical ganglion express neuropeptide Y (NPY), but few express galanin, vasoactive intestinal peptide (VIP), or substance P. However, within a few days after postganglionic nerve transection, these neurons decrease their expression of NPY and begin to express galanin, VIP, and substance P. Such changes are detected first at the mRNA level and later at the peptide level and can be localized to the principal neurons in the ganglion. Both leukemia inhibitory factor (LIF) and nerve growth factor (NGF) have been found to be involved in this phenotypic switch. LIF mRNA, though undetectable normally in peripheral ganglia and nerves, is induced in nonneuronal cells within 60 min after transection of the ganglion's main postganglionic trunks. When the effects of axotomy on peptide expression are examined in wild type and LIF-minus transgenic mice, the changes are substantially blocked in the knock out animals. Nerve transection also deprives the ganglion of target-derived NGF. Experiments in which intact animals were administered an NGF antiserum showed that loss of NGF *per se* increases expression of galanin and VIP and decreases expression of NPY. Furthermore, the increases in expression of galanin and VIP after axotomy are partially reversed *in vivo* by local application of NGF to the ganglion. Thus, the changes in peptide phenotype seen in axotomized sympathetic depend both on the induction of LIF and the removal of NGF. (Supported by NS12651 and 17512).

POSTER ABSTRACTS